AMENDMENTS TO THE CLAIMS

1-47. (Canceled)

48. (Withdrawn) A method for attenuating expression of a target gene in mammalian cells, comprising introducing into the mammalian cells a single-stranded hairpin ribonucleic acid (RNA) comprising self complementary sequences of 19 to 100 nucleotides that form a duplex region, which self complementary sequences hybridize under intracellular conditions to a target gene, wherein said hairpin RNA (i) is a substrate for cleavage by a RNaseIII enzyme to produce a double-stranded RNA product, (ii) does not produce a general sequence-independent killing of the mammalian cells, and (iii) reduces expression of said target gene in a manner dependent on the sequence of said complementary regions.

49. (Withdrawn) A method for attenuating expression of a target gene in mammalian cells, comprising introducing into the mammalian cells a single-stranded hairpin ribonucleic acid (RNA) comprising self complementary sequences of 19 to 100 nucleotides that form a duplex region, which self complementary sequences hybridize under intracellular conditions to a target gene, wherein said hairpin RNA (i) is cleaved in the mammalian cells to produce an RNA guide sequence that enters an Argonaut-containing complex, (ii) does not produce a general sequence-independent killing of the mammalian cells, and (iii) reduces expression of said target gene in a manner dependent on the sequence of said complementary regions.

50-82. (Canceled)

83. (Amended) A method for attenuating expression of one or more target genes in mammalian cells, comprising introducing into mammalian cells suspended in culture a library of single-stranded hairpin ribonucleic acid (RNA) species, each hairpin RNA species comprising self complementary sequences of 20 to 100 nucleotides that form a duplex region~~s and~~ which hybridize~~s~~ under intracellular conditions to a target gene, wherein each of said hairpin RNA species (i) is a substrate for cleavage by a RNase III enzyme to produce a double-stranded

RNA product, (ii) does not produce a general sequence-independent killing of the mammalian cells, and (iii) if complementary to a target sequence, reduces expression of said target gene in a manner dependent on the sequence of said complementary regions.

84. (Previously presented) The method of claim 83, wherein said library of hairpin RNA species collectively attenuate expression of a plurality of different target genes.

85. (Previously presented) The method of claim 83, wherein said library of hairpin RNA species are arrayed on a solid substrate.

86. (Previously presented) The method of claim 83, wherein said library of hairpin RNA species are arrayed in wells of a multi-well plate.

87. (Previously presented) The method of claim 83, including the further step of identifying hairpin RNA species of said library which produce a detected phenotype in said mammalian cells.

88. (Previously presented) The method of claim 95, wherein said promoter is an RNA polymerase III promoter or an snRNA promoter.

89. (Previously presented) The method of claim 88, wherein said promoter is an U6 promoter.

90. (Previously presented) The method of claim 83, wherein the hairpin RNA is a chemically synthesized product.

91. (Previously presented) The method of claim 83, wherein the hairpin RNA is a in vitro transcription product.

92. (Previously presented) The method of claim 83, wherein the hairpin RNA is transfected into said mammalian cells.

93. (Previously presented) The method of claim 83, wherein the hairpin RNA is microinjected into said mammalian cells.

94. (Previously presented) The method of claim 83, wherein the hairpin RNA is a transcriptional product that is transcribed from an expression construct introduced into said mammalian cells, which expression construct comprises a coding sequence for transcribing said hairpin RNA, operably linked to one or more transcriptional regulatory sequences.

95. (Previously presented) The method of claim 94, wherein said transcriptional regulatory sequences include a promoter for an RNA polymerase.

96. (Previously presented) The method of claim 95, wherein said transcriptional regulatory sequences include a promoter for a bacteriophage RNA polymerase.

97. (Previously presented) The method of claim 95, wherein said transcriptional regulatory sequences include a promoter for a cellular RNA polymerase.

98. (Previously presented) The method of claim 95, wherein said promoter is selected from the group consisting of a T7 promoter, a T3 promoter, and an SP6 promoter.

99. (Previously presented) The method of claim 94, wherein said transcriptional regulatory sequences includes an inducible promoter.

100. (Previously presented) The method of claim 94, wherein said mammalian cells are stably transfected with said expression construct.

101. (Previously presented) The method of claim 83, wherein said hairpin RNA is a transcriptional product of an RNA-dependent RNA polymerase.

102. (Previously presented) The method of claim 83, wherein the mammalian cells are germ line cells.

103. (Previously presented) The method of claim 83, wherein the mammalian cells are stem cells.

104. (Previously presented) The method of claim 83, wherein the mammalian cells are somatic cells.

105. (Previously presented) The method of claim 83, wherein the mammalian cells are immortalized cells.

106. (Previously presented) The method of claim 83, wherein the mammalian cells are primate cells.

107. (Previously presented) The method of claim 106, wherein the primate cells are human cells.

108. (Previously presented) The method of claim 83, wherein the mammalian cells are selected from the group consisting of adipocytes, fibroblasts, myocytes, cardiomyocytes, endothelium, neurons, glia, blood cells, megakaryocytes, lymphocytes, macrophages, neutrophils, eosinophils, basophils, mast cells, leukocytes, granulocytes, keratinocytes, chondrocytes, osteoblasts, osteoclasts, hepatocytes, and cells of the endocrine or exocrine glands.

109-110 (canceled).

111. (Previously presented) The method of claim 83, wherein expression of the target is attenuated by at least 33 percent relative to expression in cells not treated with said hairpin RNA.

112. (Previously presented) The method of claim 83, wherein expression of the target is attenuated by at least 90 percent relative to expression in cells not treated with said hairpin RNA.

113. (Previously presented) The method of claim 83, wherein the target gene is an endogenous gene of the mammalian cell.

114. (Previously presented) The method of claim 83, wherein the target gene is a heterologous gene relative to the genome of the mammalian cell.

115. (Previously presented) The method of claim 83, wherein the target gene is a gene of a pathogen.

116. (Previously presented) The method of claim 83, wherein the self complementary sequences hybridize under intracellular conditions to a mature mRNA transcript.

117. (Previously presented) The method of claim 83, wherein the self complementary sequences hybridize under intracellular conditions to a non-coding sequence of the target gene.

118. (Previously presented) The method of claim 83, wherein the self complementary sequences hybridize under intracellular conditions to an untranscribed sequence of the target gene, which untranscribed sequence is operably linked to the coding sequence of the target gene.

119. (Previously presented) The method of claim 83, wherein the self complementary sequences hybridize under intracellular conditions to a non-coding sequence of the target gene selected from the group consisting of promoter sequence, enhancer sequence and intronic sequence.

120. (Previously presented) The method of claim 83, wherein the self complementary sequences hybridize under intracellular conditions to a target gene selected from the group consisting of developmental genes, oncogenes, tumor suppressor genes, and genes encoding enzymes.

121. (Previously presented) The method of claim 83, wherein the hairpin RNA includes one or more modifications to phosphate-sugar backbone or nucleosides residues.

122. (Previously presented) The method of claim 121, wherein the modifications inhibit inactivation of the hairpin RNA by adenosine deaminase.

123. (Previously presented) The method of claim 83, wherein the self complementary sequences are 20-50 nucleotides in length.

124. (Previously presented) The method of claim 83, wherein the self complementary sequences are 29 nucleotides in length.